UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/721,091	11/26/2003	Terry J. Amiss	P-6011	6187

46851 7590 07/29/2005

DAVID W. HIGHET
BECTON, DICKINSON AND COMPANY
1 BECTON DRIVE, MC110
FRANKLIN LAKES, NJ 07417

EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/721,091	AMISS ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *July 5, 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *19-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-58* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/05/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O.

DETAILED ACTION

Applicants' reply filed May 9, 2005, is acknowledged.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-18, drawn to a method for quantifying analyte, classified in class 436/172, for example.

II. Claims 19-29 and 33-39, drawn to compositions and kits, classified in class 435/810, for example.

III. Claims 30-31, drawn a vector and host cell, classified in class 435/320.1, for example.

IV. Claim 32, drawn to a method for producing protein, classified in class 435/183, for example.

V. Claims 40-58, drawn to a method for quantifying analyte, classified in class

The inventions are distinct, each from the other because of the following reasons:

Inventions (I or V) and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products of Invention II can be used in a fluorescence microscopy method.

Inventions (I or V) and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a

materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products of Invention III can be used in a method for screening PBPs.

Inventions I, IV and V are independent and patentably distinct from each other. Inventions are independent and patentably distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different modes of operation and different functions. For example, Invention I requires the step of measuring resonance energy transfer, which is not required in Groups IV and V. Invention IV requires the step of culturing, which is not required in Groups I and V. Invention V requires the step of administering GGBP mutants, which is not required in Groups I and IV.

Inventions II and III are independent and patentably distinct. Inventions are independent and patentably distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different modes of operation and different functions because Invention II requires a labeling moiety, while Invention III requires a vector.

Inventions (II or III) and IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the process of Invention IV can be used to make a materially different product, such as PBP-flavored beer.

Claim 40 is generic to a plurality of disclosed patentably distinct species comprising a plurality of GGBP point mutants listed in claim 40, step a). A search for multiple protein sequences constitutes a significant burden upon the Office. Should Applicant elect Invention V in the future, Applicant will be required under

35 U.S.C. 121 to elect a single disclosed species (i.e. a single GGBP point mutant), even if this requirement is traversed. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Since applicant has received an action on the merits for the originally presented invention (i.e. Invention I), this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 19-58 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Currently, claims 1-18 are under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because the clause regarding "willful false statements ..." required by 37 CFR 1.68 has been omitted.

Claim Rejections - 35 USC § 112

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step a), the recitation of "said fusion protein has a dissociation constant of at least 1 mM towards said analyte" is indefinite because the exact experimental conditions for measurement of dissociation constants is not clear. Applicants' specification does not provide a definite standard for ascertaining the dissociation constants, such that one of ordinary skill in the art would be reasonably apprised of the scope of the invention.

In claim 1, step d), the recitation of "in the measured the luminescence value" appears grammatically awkward.

In claim 6, the repeated recitation of "and" renders the claim indefinite because it is not clear what value(s) is/are required for calculating a ratio. In addition, the recitation of "a difference in the measured luminescence value of (b)" is indefinite because it is not clear what mathematical operation is performed on said "luminescence value of (b)".

In claim 18, the recitation of proprietary trademarks (e.g. "Alexa") is indefinite.

Claim Rejections - 35 USC § 102

Claims 1-13 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Lakowicz et al. (US 6,197,534).

Lakowicz et al. teach a method for quantifying an analyte in a sample (see Abstract) comprising the steps of: administering a fusion protein to said sample (see col. 12, lines 17-19), said fusion protein comprising

a functional periplasmic binding protein (see Fig. 16), at least one labeling moiety (see Fig. 16) and at least one fluorescent protein (see Fig. 16), measuring the luminescence of said fluorescent fusion protein (see col. 6, lines 36-40) at various concentrations of analyte (see col. 2, lines 37-40, "detectable quality that changes in a concentration-dependent manner"), and determining the difference in luminescence at various concentrations of analyte (see col. 2, lines 43-44, "detecting changes in said detectable quality") due to resonance energy transfer (see col. 8, line 23).

With respect to the limitation "wherein said fusion protein has a dissociation constant of at least 1 mM towards said analyte", it appears that Applicants have not disclosed the exact experimental conditions for measurement of dissociation constants. Therefore, Examiner posits that Lakowicz et al. necessarily teach a fusion protein having a dissociation constant of at least 1 mM towards said analyte, and would be so recognized by persons of ordinary skill in the art.

With respect to claims 2-4, Lakowicz et al. teach a method wherein measurements are performed over time (see col. 4, lines 8-10, "spectral change") on a reversibly binding analyte (see col. 4, lines 8-10).

With respect to claims 6 and 8, Lakowicz et al. teach a method wherein a fluorescence ratio of the protein or labeling moiety are measured (see Example 5, "fractional fluorescence intensity").

Claim Rejections - 35 USC § 103

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lakowicz et al. (US 6,197,534) in view of Tsien & Campbell (US 2003/0059835).

Lakowicz et al. teach a method for quantifying an analyte as substantially described supra. Lakowicz et al. do not teach a method using DsRed2(C119A).

However, Tsien & Campbell teach the use of DsRed2 (see para. [0012]), including C119 mutant DsRed (see e.g. para. [0128], "C117E"), for use as a member of a donor/acceptor pair for fluorescence resonance energy transfer (see para. [0008]). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method of Lakowicz et al. with the use of DsRed2(C119A) because Tsien & Campbell discovered the importance of C119 in fluorescent protein oligomerization. Tsien & Campbell also discovered that, by mutating key amino acid residues—including C119—oligomerization can be minimized (see e.g. para. [0128], "The ultimate product of the mutagensis approach described herein is a monomeric red fluorescent protein"), which results in improved data interpretation (see para. [0010] – [0013]). Applicants' selection of a particular alanine substitution is not disclosed to be material to the patentability of Applicants' invention and does not render claim 16 patentable because such a selection of a known material on the basis of its suitability for the intended use is a matter of obvious design choice that is within the general skill of a worker in the art. In re Leshin, 125 USPQ 416 (CCPA 1960).

Response to Arguments

In prior Office Action, Examiner objected to the disclosure. Applicants' amendments to the specification and abstract are sufficient to overcome this objection. Accordingly, this objection is withdrawn.

In prior Office Action, claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps. Applicants' amendment to claim 1 is sufficient to overcome this rejection. Accordingly, this rejection is withdrawn.

In prior Office Action, claims 3, 10-11, 13, 15 and 18 were rejected under 35 U.S.C. 112, second paragraph, for various reasons. Applicants argumentation is persuasive. Accordingly, these rejections are withdrawn.

In prior Office Action, claims 1-13 and 17-18 were rejected under 35 U.S.C. 102(b) as being anticipated by Lakowicz et al. (US 6,197,534). In response, Applicants have amended claim 1 to recite the newly added limitation of "said fusion protein has a dissociation constant of at least 1 mM towards said analyte". Applicants appear to distinguish their invention from the cited prior art based on Applicants' claimed fusion proteins having weaker affinity towards their target ligands (see Applicants' reply, p. 20, last paragraph, first sentence). Applicants' arguments have been carefully considered but are not persuasive because it appears that Applicants have not disclosed the exact experimental conditions for measurement of dissociation constants. Thus, Examiner posits that Lakowicz et al. necessarily teach a fusion protein having a dissociation constant of at least 1 mM towards said analyte, and would be so recognized by persons of ordinary skill in the art.

In prior Office Action, claims 14-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lakowicz et al. (US 6,197,534) in view of Tsien & Campbell (US 2003/0059835). In response, Applicants argue that Tsien & Campbell describe a cysteine mutation "at an entirely different position in an entirely different protein" (see Applicants' reply, p. 22, first full paragraph, second full paragraph). Applicants' argument has been carefully considered but is not persuasive because the DsRed protein described by Tsien & Campbell is not an entirely different protein from the DsRed2 protein claimed by Applicants. The DsRed2 protein claimed by Applicants was derived from DsRed protein, such that a person of ordinary skill would have recognized that the amino acid sequences of DsRed2 and DsRed are nearly identical, and that C119 of DsRed2 is homologous to C117 of DsRed.

In addition, Applicants argue that the decision in *In re Leshin* does not apply here because alanine is not a known substitute for glutamate (see Applicants' reply, p. 22, second full paragraph). Applicants'

argument has been carefully considered but is not persuasive because, it appears that Applicants' selection of a particular alanine substitution is not so important, so long as the cysteine sulfhydryl functionality of residue 119 is removed. In other words, the intended use of the particular alanine substitution is to remove the cysteine sulfhydryl functionality of residue 119. Where Applicants' selection of a particular amino acid substitution is not disclosed to be material to the patentability of Applicants' invention, any known amino acid substitution resulting in removal of the cysteine sulfhydryl functionality of residue 119, e.g. alanine and glutamate, satisfies Applicants' intended purpose and are known substitutes.

In prior Office Action, claims 1-18 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable in view of copending Application No. 10/040,077. Applicants have informed Examiner that copending Application No. 10/040,077 has matured into US 6,855,556. Claims drawn to methods for quantifying analyte are not recited in US 6,855,556. Accordingly, this rejection is withdrawn.

In prior Office Action, claims 1-18 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable in view of copending Application No. 10/039,833. Applicants have informed Examiner that copending Application No. 10/039,833 has been abandoned. Accordingly, this rejection is withdrawn.

Double Patenting

Claims 1-13 and 17-18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-24, 38 and 41 of copending Application No. 10/776,643 in view of Lakowicz et al. (US 6,197,534).

The '643 application claims a method for quantifying an analyte (see claim 22, "glucose detection") comprising the steps of administering a protein comprising a periplasmic binding protein (see claim 22, "glucose/galactose binding protein") and at least one labeling moiety (see claim 22, "reporter group"), and measuring the luminescence of said protein (see claim 38, "luminescent label"). The '643 application does not claim a method comprising "at least one fluorescent protein."

However, Lakowicz et al. teaches a method for quantifying an analyte comprising the steps of administering a fusion protein comprising at least one fluorescent protein (see Fig. 16). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the claims of the '643 application to include a fluorescent protein because Lakowicz et al. teaches that GGBP-GFP fusion proteins produces useful spectral changes upon glucose binding, which allow for real-time glucose measurements by fluorescence resonance energy transfer (see col. 6, lines 26-35).

Claims 14-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-24, 38 and 41 of copending Application No. 10/776,643 and Lakowicz et al. (US 6,197,534) as applied to claims 1 and 13, and further in view of Tsien & Campbell (US 2003/0059835).

The '643 application and Lakowicz et al. teach a method for quantifying an analyte as substantially described supra. The '643 application does not claim a method using DsRed2(C119A).

However, Tsien & Campbell teach the use of DsRed2 (see para. [0012]), including C119 mutant DsRed (see e.g. para. [0128], "C117E"), for use as a member of a donor/acceptor pair for fluorescence resonance energy transfer (see para. [0008]). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the claims of the '643 application to include the use of DsRed2(C119A) because Tsien & Campbell discovered the importance of C119 in fluorescent protein oligomerization. Tsien & Campbell also discovered that, by mutating key amino acid residues—including C119—

oligomerization can be minimized (see e.g. para. [0128], "The ultimate product of the mutagensis approach described herein is a monomeric red fluorescent protein"), which results in improved data interpretation (see para. [0010] – [0013]). Applicants' selection of a particular alanine substitution is not disclosed to be material to the patentability of Applicants' invention and does not render claim 16 patentable because such a selection of a known material on the basis of its suitability for the intended use is a matter of obvious design choice that is within the general skill of a worker in the art. In re Leshin, 125 USPQ 416 (CCPA 1960).

These are provisional obviousness-type double patenting rejections.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be

reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci
Examiner
Art Unit 1641

djv

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
07/25/05